PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	FOR FURTHER ACTION	see Form PCT/ISA/220 as well as, where applicable, item 5 below.
X16538		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/US2005/007507	09/03/2005	22/03/2004
Applicant		
ELI LILLY AND COMPANY		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 8 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report

1. **Basis of the report**
   a. With regard to the **language,** the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
      [ ] The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
   b. [ ] With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. [ ] **Certain claims were found unsearchable** (See Box II).

3. [ ] **Unity of invention is lacking** (see Box III).

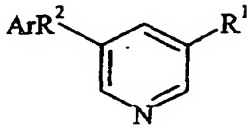
4. With regard to the **title,**
   [X] the text is approved as submitted by the applicant.
   [ ] the text has been established by this Authority to read as follows:

5. With regard to the **abstract,**
   [ ] the text is approved as submitted by the applicant.
   [X] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the **drawings,**
   a. the figure of the **drawings** to be published with the abstract is Figure No. _____
      [ ] as suggested by the applicant.
      [ ] as selected by this Authority, because the applicant failed to suggest a figure.
      [ ] as selected by this Authority, because this figure better characterizes the invention.
   b. [ ] none of the figures is to be published with the abstract.

Box No. IV Text of the abstract (Continuation of item 5 of the first sheet)

The present invention is directed toward pyridyl derivatives of formula (I) as antagonists of the mGlu5 receptor. As such the compounds may be useful for treatment or prevention of disorders remedied by antagonism of the mGlu5 receptor.



(I)

wherein

Ar is phenyl or napthyl each of which may be substituted by one or more C_1-C_4 alkyl, C_1-C_4 alkoxy, C_1-C_5 acyl, halo, amino, nitro, cyano, hydroxy, C_1-C_5 acylamino, C_1-C_4 alkylsulfonylamino, mono-, di- or trifluorinated C_1-C_3 alkyl, substituents which may be the same or different and may bear a $CONH_2$, $CONHCH_3$, $CON(CH_3)_2$, CO_2H, CO_2CH_3, OCF_3, $CH_2NHCOCH_3$, CH_2NH_2, $CH_2N(CH_3)_2$, CH_2CN, CH_2OH, $CH_2NHSO_2CH_3$, $CH_2N(CH_3)(CH_2)_2$ CN, $CH_2N(CH_3)CH(CH_3)_2$, $CH_2NHCH(CH_3)_2$, $CH_2NH(CH_2)_2CH_3$, $CH_2NHCO_2R^4$, $CH_2NHCH_2CH_3$, CH_2NHCH_3, $NHCOC(CH_3)_2$, or $N(S(O)_2CH_3)_2$ substituent;

R^1 is hydrogen, halo, R^4, CN, $C(NOH)R^3$, $C(NO\text{-}R^4)R^3$, $(CH)_2CO_2R^4$, $(CH_2)_n OR^3$, COR^3, CF_3, SR^4, $S(O)R^4$, $S(O)_2R^4$, $COCH_2CO_2R^3$, $NHSO_2R^4$, $NHCOR^3$, $C(NOR^3)NH_2$, CH_2OCOR^3, $(CH_2)_n NH_2$, $CON(CH_3)_2$, $(CH_2)_nNHCO_2R^4$, CO_2R^3, $CONH_2$, $CSNH_2$, $C(NH)NHOR^3$, $(CH_2)_nN(CH_3)_2$, or $CONHNHCOR^3$;

R^2 is 1,2-ethenediyl or 1,2-ethynediyl;

R^3 is hydrogen or C_1-C_4 alkyl;

R^4 is C_1-C_4 alkyl; and

n is 0, 1, 2, 3 or 4;

or a pharmaceutically acceptable salt thereof; or an N-oxide thereof.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US2005/007507

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K31/4406 A61K31/44 C07D213/16 C07D213/18 C07D213/85
C07D213/89 C07D213/61 C07D213/65 A61P25/28 A61P29/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, CHEM ABS Data, WPI Data, PAJ, BEILSTEIN Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	✓WO 01/90101 A (AVENTIS PHARMACEUTICALS PRODUCTS INC; ASTLES, PETER, C; EASTWOOD, PAUL) 29 November 2001 (2001-11-29) see page 161, line 4	5,6, 10-12, 18,20
X	✓HOEKSTRA ET AL: "Potent, Orally Active GPIIb/IIIa Antagonists Containing a Nipecotic Acid Subunit. Structure-Activity Studies Leading to the Discovery of RWJ-53308" JOURNAL OF MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY. WASHINGTON, US, vol. 42, no. 25, 1999, pages 5254-5265, XP002142349 ISSN: 0022-2623 see 18a, scheme 5	5,6, 10-13, 18,20

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance, the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
14 June 2005	27. 07. 05

Name and mailing address of the ISA	Authorized officer
European Patent Office, P B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Scruton-Evans, I

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Form PCT/ISA/210 (second sheet) (January 2004)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 96/01825 A (FUJISAWA PHARMACEUTICAL CO., LTD; HEMMI, MITSUE +HF; SHIMAZAKI, NORIHI) 25 January 1996 (1996-01-25) see preparation 101,102, pages 133,134 and formula XIIb, page 18	5-10,12, 13,15, 19,20
X	WO 97/24355 A (FUJISAWA PHARMACEUTICAL CO., LTD; SHIMAZAKI, NORIHIKO; SAWADA, AKIHIKO) 10 July 1997 (1997-07-10) see preparation 2, page 47 and preparation 6, page 49	5-10,12, 15,19,20
P,X	SORENSEN U S ET AL: "Copper-free palladium-catalyzed sonogashira-type coupling of aryl halides and 1-aryl-2-(trimethylsilyl)acetylenes" TETRAHEDRON, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 61, no. 10, 7 March 2005 (2005-03-07), pages 2697-2703, XP004756737 ISSN: 0040-4020 see compound 2, Table 1, compounds 15,16 page 2700	5-7,10, 12,19,20
X	NOVAK, ZOLTAN ET AL: "Tandem Sonogashira coupling: An efficient tool for the synthesis of diarylalkynes" ORGANIC LETTERS , 6(26), 4917-4920 CODEN: ORLEF7; ISSN: 1523-7060, 12 February 2004 (2004-02-12), XP002331794 see pages 5,7,8	5-10,12, 16,19,20
P,X	WOLF, CHRISTIAN ET AL: "Palladium-phosphinous acid-catalyzed Sonogashira cross-coupling reactions in water" ORGANIC & BIOMOLECULAR CHEMISTRY , 2(15), 2161-2164 CODEN: OBCRAK; ISSN: 1477-0520, 30 June 2004 (2004-06-30), XP002331795 see Table 2, compounds 18,20	5-10,12, 16,19,20
P,X	HE H ET AL: "Copper-catalyzed cross-coupling of aryl iodides and aryl acetylenes using microwave heating" TETRAHEDRON LETTERS, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 45, no. 16, 12 April 2004 (2004-04-12), pages 3237-3239, XP004498987 ISSN: 0040-4039 see entry o, table 1, page 3238	5-8,10, 12,19,20

-/--

1

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	✓PENNEY J M ET AL: "Alkynylation of benzonitriles via nickel catalyzed C-C bond activation" TETRAHEDRON LETTERS, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 45, no. 25, 14 June 2004 (2004-06-14), pages 4989-4992, XP004510991 ISSN: 0040-4039 see entry 6, Table 1	5-10,12, 16,19,20
P,X	✓SUN, SHIH-SHENG ET AL: "Directed Assembly of Transition-Metal-Coordinated Molecular Loops and Squares from Salen-Type Components. Examples of Metalation-Controlled Structural Conversion" JOURNAL OF THE AMERICAN CHEMICAL SOCIETY , 126(20), 6314-6326 CODEN: JACSAT; ISSN: 0002-7863, 2004, XP002331796 see page 6315 experimental3-tbu-5-(3'-ethynylpyridyl)-2-OH benzaldehyde	5-8,10, 12,19,20
X	✓ RAJADURAI, CHANDRASEKAR ET AL: "Study on the Heteroatom Influence in Pyridine-Based Nitronyl Nitroxide Biradicals with Phenylethynyl Spacers on the Molecular Ground State" JOURNAL OF ORGANIC CHEMISTRY , 68(26), 9907-9915 CODEN: JOCEAH; ISSN: 0022-3263, 2003, XP002331797 se compound 10, figure 2	5-8, 10-12, 18-20
X	✓ KATRITZKY, ALAN R. ET AL: "The preparation of diarylacetylenes via diphenyl (benzotriazol-1-yl)(aryl)methylphosphonates" ARKIVOC (GAINESVILLE, FL, UNITED STATES) , (13), 17-27 CODEN: AGFUAR URL: HTTP://WWW.ARKAT-USA.ORG/ARK/JOURNAL/2002/KARABATSOS/GK-706F/706F.PDF, 2002, XP002331798 see entry 11, Table 2 and experimental, page 26, last compound	5-10,12, 19,20
X	✓ WO 03/035620 A (ASAHI KASEI KABUSHIKI KAISHA; MIYOSHI, SHIRO; OGAWA, KOHEI) 1 May 2003 (2003-05-01) see reference example 9A & EP 1 447 400 A (ASAHI KASEI PHARMA CORPORATION) 18 August 2004 (2004-08-18)	5-8,10, 12,16, 19,20

-/--

1

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PCT/US2005/007507

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	✓WANG, ZHIYONG ET AL: "An improved coupling reaction for the preparation of pyridylethynyl benzonitrile compounds" CHINESE SCIENCE BULLETIN , 46(19), 1606-1608 CODEN: CSBUEF; ISSN: 1001-6538, 2001, XP009048572 see compounds 6a,6c	5-10,12, 19,20
X	✓LIN, WENBIN ET AL: "Three-Dimensional Manganese(II) Coordination Polymers Based on m-Pyridinecarboxylates: Synthesis, X-ray Structures, and Magnetic Properties" INORGANIC CHEMISTRY , 39(18), 4169-4173 CODEN: INOCAJ; ISSN: 0020-1669, 2000, XP002331799 see page 4169, Scheme 1, last line page 4170 and reference 22	5-8,10, 12,16, 19,20
P,X	✓CRYSTAL GROWTH AND DESIGN, vol. 5, no. 2, 14 September 2004 (2004-09-14), pages 609-616, XP002331800 see compound 3 page 610 ART MALLIK	5-7,9, 10, 12-14, 19,20
X	✓EP 0 436 398 A (ALLERGAN, INC) 10 July 1991 (1991-07-10) cited in the application see formula I definitions	5
A	✓WO 01/16121 A (MERCK & CO., INC; COSFORD, NICHOLAS, D., P; MCDONALD, IAN, A; BLEICHER) 8 March 2001 (2001-03-08) cited in the application the whole document	1-25
A	WO 01/72291 A (THE VICTORIA UNIVERSITY OF MANCHESTER; BROTCHIE, JONATHAN; HILL, MICHA) 4 October 2001 (2001-10-04) cited in the application the whole document	1-25
P,A	✓WO 2004/067002 A (RECORDATI S.A; RECORDATI INDUSTRIA CHIMICA E FARMACEUTICA S.P.A) 12 August 2004 (2004-08-12) see formula I	1-25

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US2005/007507

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 0190101 A	29-11-2001	AU 5741301 A	03-12-2001
		BR 0111206 A	15-04-2003
		CA 2409827 A1	29-11-2001
		CN 1439003 A	27-08-2003
		EP 1296972 A1	02-04-2003
		HU 0302485 A2	29-12-2003
		JP 2004510697 T	08-04-2004
		MA 25809 A1	01-07-2003
		MX PA02011400 A	23-05-2003
		NO 20025601 A	06-01-2003
		PL 360495 A1	06-09-2004
		WO 0190101 A1	29-11-2001
		US 2003187020 A1	02-10-2003
		ZA 200209484 A	23-02-2004
WO 9601825 A	25-01-1996	AT 232531 T	15-02-2003
		AU 698133 B2	22-10-1998
		AU 2899295 A	09-02-1996
		CA 2194872 A1	25-01-1996
		CN 1157617 A ,C	20-08-1997
		CN 1250776 A	19-04-2000
		DE 69529614 D1	20-03-2003
		DE 69529614 T2	03-07-2003
		DK 770079 T3	10-06-2003
		EP 0770079 A1	02-05-1997
		EP 0920867 A1	09-06-1999
		ES 2187561 T3	16-06-2003
		HK 1004483 A1	24-10-2003
		HU 77353 A2	30-03-1998
		WO 9601825 A1	25-01-1996
		JP 3206003 B2	04-09-2001
		JP 10502630 T	10-03-1998
		PT 770079 T	30-06-2003
		RU 2170737 C2	20-07-2001
		TW 383307 B	01-03-2000
		US 2002107251 A1	08-08-2002
		US 6426345 B1	30-07-2002
WO 9724355 A	10-07-1997	AT 214067 T	15-03-2002
		AU 720301 B2	25-05-2000
		AU 1111297 A	28-07-1997
		CA 2241690 A1	10-07-1997
		CN 1205702 A ,C	20-01-1999
		DE 69619702 D1	11-04-2002
		DE 69619702 T2	14-08-2002
		DK 874845 T3	01-07-2002
		EA 1324 B1	26-02-2001
		EP 0874845 A1	04-11-1998
		ES 2170286 T3	01-08-2002
		HU 9901038 A2	28-07-1999
		IL 124673 A	25-07-2002
		WO 9724355 A1	10-07-1997
		JP 2000502699 T	07-03-2000
		PT 874845 T	30-08-2002
		US 6117875 A	12-09-2000
WO 03035620 A	01-05-2003	CA 2464367 A1	01-05-2003
		EP 1447400 A1	18-08-2004

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US2005/007507

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 03035620 A		WO 03035620 A1	01-05-2003
		US 2005020602 A1	27-01-2005
EP 1447400 A	18-08-2004	CA 2464367 A1	01-05-2003
		EP 1447400 A1	18-08-2004
		US 2005020602 A1	27-01-2005
		WO 03035620 A1	01-05-2003
EP 0436398 A	10-07-1991	US 5013744 A	07-05-1991
		AT 133665 T	15-02-1996
		AU 642183 B2	14-10-1993
		AU 6828490 A	04-07-1991
		CA 2031480 A1	30-06-1991
		DE 69025157 D1	14-03-1996
		DE 69025157 T2	14-11-1996
		EP 0436398 A1	10-07-1991
		ES 2081951 T3	16-03-1996
		IE 904710 A1	17-07-1991
		JP 7173136 A	11-07-1995
		US 5414007 A	09-05-1995
		US 5516904 A	14-05-1996
		US 5175185 A	29-12-1992
		US 5264456 A	23-11-1993
WO 0116121 A	08-03-2001	AU 780009 B2	24-02-2005
		AU 6948200 A	26-03-2001
		CA 2383524 A1	08-03-2001
		EP 1214303 A1	19-06-2002
		JP 2003508390 T	04-03-2003
		WO 0116121 A1	08-03-2001
		US 2003055247 A1	20-03-2003
		US 2005043307 A1	24-02-2005
		US 2005085523 A1	21-04-2005
WO 0172291 A	04-10-2001	AU 4256801 A	08-10-2001
		AU 2001242568 B2	04-11-2004
		CA 2404049 A1	04-10-2001
		EP 1274417 A2	15-01-2003
		WO 0172291 A2	04-10-2001
		JP 2003528136 T	24-09-2003
		US 2003109504 A1	12-06-2003
WO 2004067002 A	12-08-2004	WO 2004067002 A2	12-08-2004
		US 2004215284 A1	28-10-2004